

Amendments to the Specification:

Add the following new paragraph at page 1, line 4, before the heading "Technical Field":

Cross Reference to Related Applications

This application is a continuation of U.S. Application Serial No. 09/830,548, filed June 12, 2001, which is a U.S. National Phase Application of PCT Application No. PCT/JP00/05868, filed August 30, 2000, which claims priority to Japanese Application Serial No. 2000/254680, filed August 24, 2000, and Japanese Application Serial No. 11/242672, filed August 30, 1999. The disclosures of the prior applications are considered part of (and are incorporated by reference in) the disclosure of this application.

Replace the paragraph beginning at page 4, line 18 with the following amended paragraph:

The ligands for CD28 and CTLA-4 are CD80 (B7-1) and CD86 (B7-2) in human and mice. CTLA-4 has about 20 times as high affinity to both ligands as CD28. It has been elucidated that the amino acid sequence structures "MYPPPY (Met-Tyr-Pro-Pro-Pro-Tyr; SEQ ID NO:1)" conserved through animal species is important for the binding of CD28 and CTLA-4 to CD80 (B7-1). It has also been reported that, when CD28 is stimulated, PI3 kinase (phosphoinositide 3 kinase, PI3K) associates with the phosphorylated tyrosine residue in a partial sequence "YMNM (Tyr-Met-Asn-Met; SEQ ID NO:2)" of CD28 and that CD28 plays an important role in intracellular signal transmission through this "YxxM" structure. Furthermore, it has been reported that CTLA-4 also has a sequence represented by "YxxM," namely "YVKM (Tyr-Val-Lys-Met; SEQ ID NO:3)" in its cytoplasmic region and that, after being stimulated, SYP associates with this sequence.